Group II: Claims 1-6, 9, 17-23 and 26-28, drawn to compounds wherein R^5 and R^6 forms a ring.

In addition, the Office has required the election of single disclosed species for the elected group.

Applicants note that the PCT administrative instructions, Annex B, Part 1(f) indicates that the alternatives defined in a single claim shall meet the technical relationship requirements of PCT Rule 13.2 if they are of a "similar nature", as defined by the following criteria:

(A) all the alternatives have a common property or activity, and

(B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives.

Applicants submit that criteria (A) and (B)(1) are met since the compounds share a common property: treatment and/or prevention of disorders of the autoimmune and neuronal system (page 1, lines 9-10); and share a common structural feature: formula I. Accordingly, they are of a "similar nature".

In addition, Applicants traverse that Restriction Requirement on the grounds that the Office has not applied the same standard of unity of invention as the International Searching Authority (see copy of the International Preliminary Examination Report appended herewith). The Authority did not take the position that unity of invention was lacking in the International application and examined all claims together. Applicants note that PCT Article 27(l) states:

> No national law shall require compliance with requirements relating to the form or contents of the international application different from or additional to those which are provided for in this Treaty and the Regulations.

Moreover, Applicants respectfully traverse on the grounds that the Office has not shown that a burden exists in searching the entire application.

MPEP in §803 states as follows:

> If the search and examination of an entire application can be made without a serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions.

Applicants respectfully submit that a search of all the claims would not impose a serious burden on the Office. In fact, the International Searching Authority has searched all of the claims together.

Therefore, for the reasons presented above, Applicants submit that the Office has failed to meet the burden necessary in order to sustain the Restriction and Election of Species Requirement. Withdrawal of the Restriction and Election of Species Requirement is respectfully requested.

Applicants respectfully submit that the above-identified application is now in condition for examination on the merits, and early notice of such action is earnestly solicited

Respectfully submitted,

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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

MOINAS, Michel
Moinas Savoye & Cronin
42, rue Plantamour
CH-1201 Geneva
SUISSE

REÇU le
24 DEC. 2001

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	20.12.2001
Applicant's or agent's file reference	IMPORTANT NOTIFICATION
10640WO	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB00/01382	28/09/2000	28/09/1999

Applicant
APPLIED RESEARCH SYSTEMS ARS HOLDING N.V. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49.89 2399 - 4465	Houyez-Stevens, M Tel.+49 89 2399-8163

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
10640WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB00/01382	28/09/2000	28/09/1999
International Patent Classification (IPC) or national classification and IPC C07D409/12		
Applicant APPLIED RESEARCH SYSTEMS ARS HOLDING N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20/04/2001	20.12.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Seufert, G Telephone No. +49 89 2399 8330

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB00/01382

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-39 as originally filed

Claims, No.:

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 13-16 with regard to industrial applicability; 1-8, 10-19 partly.

because:

☒ the said international application, or the said claims Nos. 13-16 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-8 10-19 partly.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4-12
	No:	Claims	1-5, 13-16, 17-19
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-19
Industrial applicability (IA)	Yes:	Claims	1-12, 18, 19

No: Claims 13-16

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

D1 Indian J. Chem., 37B, 1998, 1059-62
D2 J. Serb. Chem. Soc 63(5), 1998, 371-77
D3 CA-abstract, 119:226388 & Al-Azhar Bull. Sci. 3(1), 1992, 9.17
D4 J. Serb. Chem. Soc. 56(6), 1991, 311-18
D5 FR-A-2312242
D6 WPI-abstract, AN 1999-566553 & JP-11246527
D7 WPI-abstract, AN 1999-594027 & JP-11236369
D8 WO-A-9942443
D9 WO-A-9839329
D10 WO-A-9803166
D11 EP-A-757984
D12 WO-9849188

III. Non establishment of opinion

Independent claims 13-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT (the wording "use of a compound for the treatment" is equal to the wording "method of treatment"). Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

Furthermore, according to Rule 66.1e the International Preliminary Examination Authority is not required to carry out an examination on subject-matter for which no search report as been established.
The applicant has been informed by the Search Authority that the scope of the claims is not clear and that the search report has been established for compounds with R^3 and/or R^4 as a side chain of an amino acid. Consequently, the examination of the present invention with regard to novelty, inventive step and industrial applicability has only been carried out for that group of compounds.

V. Reasoned statement under Art. 35(29 PCT with regard to novelty, inventive step and industrial applicability

Novelty

Claim 1 of the present application refers to sulfonyl amino acid compounds of the general formula (I). Compounds falling within the scope of claim 1 are anticipated by the documents D1-D11 (see especially the registry numbers mentioned in the International search report and the general formulae of D7-D11). Therefore, claim 1 and the dependent claims 3-5 are not considered to meet the requirement of Art. 33(2) PCT. Attention is drawn to the fact that with regard to the general formulae of D7-D11 no new technical feature is apparent for the subject-matter of the overlapping area. "A new technical feature" is to be understood as a structural difference in the molecular formula of the present application.

Claim 2 refers to sulfonyl amino acid derivatives of the general formula I for use as a medicament. Such a claim only meets the criteria of novelty if none of the compounds falling within the general formula is known for a pharmaceutical activity. However, compounds falling within the general formula and having a pharmaceutical activity are known in the art, for example antibacterial activity (see D1-D4) or matrix metalloproteinase inhibitors (see D6-D11). Consequently, claim 2, its dependent claims 3-5 as well as claim 17 are not considered to comply with the requirements of Art. 33(2) PCT.

Claims 13-16 refer to the use of compounds of the formula I for the treatment of neuronal disorders, autoimmune diseases, cancer and cardiovascular diseases. Compounds falling within the scope of formula I and having the claimed activity are known in the art (see D6, or D8-D11, passages cited in the international search report). Therefore, claims 13-16 are not considered to be novel in the sense of Art. 33(2) PCT. The expression "in particular according to any of claims 10-12" are not considered to be limiting.

Inventive step

Without a clear limitation of the presently claimed subject-matter from the state of

the art, a complete examination with regard to an inventive step is not possible. However, the following preliminary remarks can already be made.

The term "substituted" employed throughout the claims (for example, substituted alkyl, alkoxy, aryl, heteroaryl, etc.) commonly includes compounds substituted by absolutely everything. Irrespective of the fact that this is not sufficiently supported by the application (Art. 6 PCT), it is not credible that the presence of just any type of substituent will result in compounds with the desired activity, which effectively means that the underlying technical problem will not be solved over basically the whole scope of the claims. Therefore, the present claims are not considered to meet the requirements of Art. 33(3) PCT.

Claims 18 and 19 are analogy processes. They are only considered to be novel or inventive in combination with a novel and inventive compound claim.

Industrial applicability

For the assessment of the present claims 13-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

VII. Certain defects

1. In the claims 1, 2, 4 and 10 the term "acylamino" has been mentioned twice for the same variables (R^3, R^4, R^6, substituent for Ar^1 and Ar^2).

2. In claim 6 the word saturated before the "cyclic C_4-C_8-alkyl"is missing (see claim 1 and 2).

3. The expression "and the like" see page 5-7 should have been deleted.

VIII. Certain observations

1. The scope of claim 1 and 2 is unclear (Art. 6 PCT) with regard to the definition of R^3 and R^4. For example, said variables are defined as "natural or synthetic amino acid residues, hydrogen, substituted or unsubstituted alkyl..., sulfoxy or sulfonyl". However, the difference between the definition of a natural or a synthetic amino acid residue and for example hydrogen or alkyl, which may be substituted, is not clear insofar as hydrogen or (substituted) alkyl are residues of natural amino acids, like glycine, alanine, phenylalanine etc. and any of the other substituents mentioned, which would not fall under the definition of a natural amino acid residue would be included by the expression "synthetic amino acid residue". Furthermore, the expression " comprising hydrogen" (see "comprising or consisting of natural or synthetic amino acid residues, hydrogen...") apparently includes almost all the other residues mentioned, since most of them have a hydrogen atom in their structure
   Equally unclear in that context is the proviso "at least one of R^3 and/or R^4 must be an amino acid residue". The applicant is requested to clarify the scope of R^3 and R^4.

2. A similar objection with regard to the expression "comprising hydrogen" is valid for the substituent R^6 in claim 1 and 2 and the substituents R^3, R^4 and R^6 in claims 6 and 10 respectively.

3. Dependent claim 4 is inconsistent with claim 1 (Art. 6 PCT). In claim 1 Ar^1 and Ar^2 are defined as aryl or heteroaryl. In claim 4 the same substituents are defined as a group comprising or consisting of phenyl, thienyl, furyl and pyridyl. A phenethyl group satisfy the requirement of "comprising a phenyl group", but is not included in the definition of claim 1.

4. The expressions "like trihalomethyl", "preferably 4-chlorophenyl", "e.g. a C_1-C_6-alkylamino aryl, a C_1-C_6-alkylamino heteroaryl" and "e.g. an unsubstituted or substituted piperidino group" in claims 1, 2, 4, 6, 7 and 10 respectively, describe only optional features, which do not limit the claims in any way. For the sake of conciseness and clarity (Art. 6 PCT) these optional features should be removed from the claims.

5. The terms "alkoxy" or "thioalkoxy" in their common technical meaning describe OR- or SR-residues whereby R is equal to an alkyl group. The definition on page 7 of the description is inconsistent with said common technical meaning. This inconsistency between the claims and the description leads to doubt concerning the matter for which protection is sought, thereby rendering the claims unclear (Article 6 PCT). A similar argument is valid for the term alkoxcarbonyl (-C(=O)OR with R = alkyl).

6. The embodiments of the invention described on page 10, lines 20-21, i.e. pharmaceutically active derivatives, does not fall within the scope of the claims. This inconsistency between the claims and the description leads to doubt con- cerning the matter for which protection is sought, thereby rendering the claims un- clear (Article 6 PCT). Furthermore, this definition does not meet the requirement of Art. 6 PCT in that it is not clear to what type of structures it refers and that it tries to define the subject-matter by the result to be achieved.

New U.S. PCT Application Based on PCT/IB00/01382
Docket No: 220316US0PCT

STATEMENT OF RELEVANCY

1) References AO-AZ have been cited in the International Search Report. Copies of these references are being submitted herewith only when not automatically provided by the International Searching Authority.

2) References_____ have been cited in the corresponding _____ Search Report. A copy of these references is being submitted herewith.

3) References AAA-AAE are discussed in the specification. A copy of these references is being submitted herewith.

4) References _____are additional prior art known to Applicant. A copy of these references is being submitted herewith.